A DNA plasmid melanoma cancer vaccine, SCIB1, combined with nivolumab + ipilimumab in patients with advanced unresectable melanoma: Efficacy and safety results from the open-label Phase 2 SCOPE trial

Heather Shaw[1-2], Poulam Patel[3], Miranda Payne[4], Satish Kumar[5], Sarah Danson[6], Martin Highley[7], Clare Barlow[8], Robert Miller[9], Fayaz Master[9] and Lindy Durrant[9]

Background

- Targeting of melanoma by T cells drives anti-tumour responses
- SCIB1 (a DNA vaccine) incorporating T cell epitopes from TRP-2 and gp100 into an antibody framework allows Fc targeting of activated dendritic cells (see figure 1)
- SCIB1 has a dual mechanism of action. Injection of SCIB1 results in:
  - the uptake of the plasmid and expression of the engineered antibody by antigen-presenting cells. The antigen is processed, and epitopes presented on either MHC class or II molecules, which react with the T cell receptor of CD8 or CD4 cells (see figure 2). This is known as direct presentation, and
  - secretion of an engineered human IgG1 antibody molecule containing the CD8 and CD4 epitopes. This fusion protein targets the CD64 FcγR present on dendritic cells via the heavy chain Fc region, resulting in uptake and cross-presentation of the epitopes to CD8 and CD4 T cells.
- A previous clinical trial of SCIB1 monotherapy in patients with unresectable and resectable melanoma demonstrated objective response and a favourable recurrence free survival rate respectively [1]

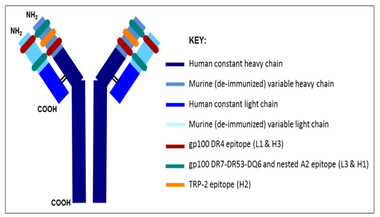

Figure 1.Engineered antibody structure

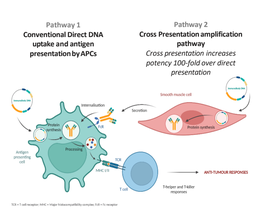

Figure 2. Mechanism of Action

Study Design

- This is a Phase 2a multicenter, multicohort, open-label study of the SCIB1 vaccine with ipilimumab plus nivolumab (cohort 1) or pembrolizumab (cohort 2). See figure 3.
- Eligible patients with stage IIIB/IV unresectable melanoma in whom standard of care checkpoint inhibitor therapy was planned, were recruited and vaccinated with 8mg SCIB1 using a needle-free injections system (Pharmajet).
- RECIST 1.1 overall response rate is the primary endpoint, and the study is designed with a Simon's two stage methodology with an early stooping rule for futility.
- Cohort 1 has been powered at 80% to detect a 20% improvement over the historical observations of 50% when the doublet checkpoints are administered in the real-world setting.
- Cohort 2 has also been powered to detect a 20% improvement over the historical observation of 35% when pembrolizumab monotherapy is administered as the standard of care in this setting.
- Cohort 1 required 9/15 responders for non-futility and an overall 27/43 patients to respond.

Study Schema

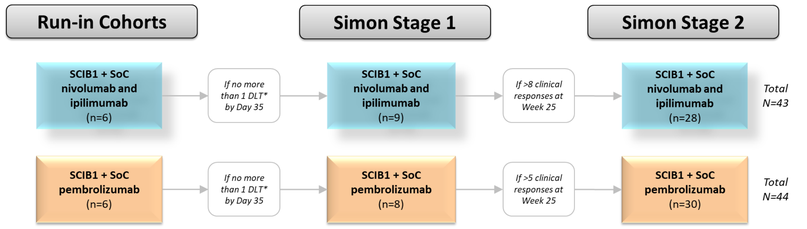

Figure 3. SCOPE Study Schema

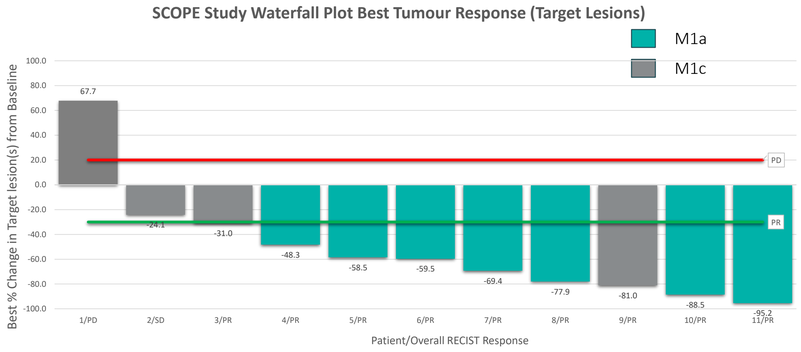

Figure 4. Water Plot

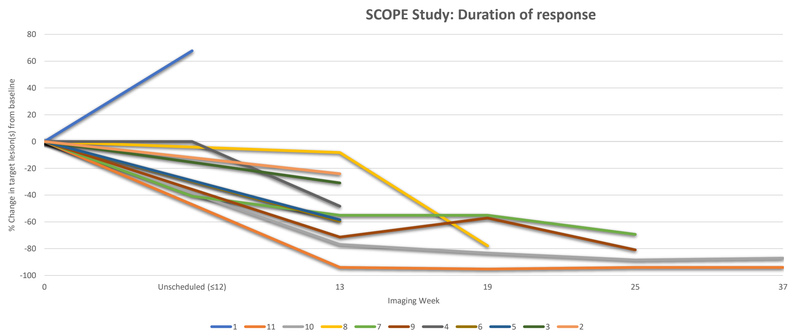

Figure 5 Spider Plot

Evaluable Patients Only		
	Number of patients (n)	
	Cohort 1:SCIB1+ipi-nivo	Cohort 2: SCIB1+pembro
Gender		
Male	8	1
Female	3	2
Age		
<65	9	0
≥65- <75	0	0
≥75	2	3
Stage of disease at study entry		
IV	11	3
M1a	7	1
M1b	0	1
M1c	4	1
Braf		
Mutation	6	1
Wildtype	5	2
Lactate Dehydrogenase		
>Upper limit of normal	7	1
≤ULN	4	0
Total Tumour Burden		
≥20 mm – ≤40mm	3	2
≥41 mm -≤80mm	3	0
≥81mm-≤150mm	4	0
150mm+	1	1
Prior treatment in the adjuvant setting		
Yes	4	1
Pembrolizumab	2	1
Nivolumab	1	0
Dabrafenib and Trametinib	1	0
No	7	2

Table 1 Demographics and Baseline Disease Characteristics

Results

As of early October 2023:

- 17 pts in whom the combinations of ipilimumab with nivolumab was planned (cohort 1), were vaccinated with 8mg SCIB1 i.m. using a needle free injections system (Pharmajet).
- 11 patients in cohort 1, had reached at least the first imaging timepoint at 13 weeks post-vaccination.
- Patients were vaccinated with SCIB1 8mg I.m. at weeks 0, 7, 13,19,25 and q12 weeks until 2 years.
- 9/11 patients had a RECIST 1.1 objective response an **82% ORR,** see figure 4.
- All patients imaged beyond week 13 showed a **sustained shrinkage** of their target lesions, see figure 5.
- SCIB1 was well tolerated when given in combination with ipilimumab and nivolumab; 116 adverse events were reported and only 16 were related to SCIB1. Of these, only one was Grade 3 the other events were mild to moderate in severity. There were no SAEs related to SCIB1.

Discussion

This poster focusses on cohort 1 as it had reached an important milestone in the completion of the first stage of Simon in a 2-stage design. When SCIB1 was included to the standard of care regimen of ipilimumab with nivolumab, the overall size of metastatic melanoma lesions had reduced significantly in 9/11 patients, yielding a RECIST 1.1 overall response rate of 82%. Due to the target of 9 responses being achieved earlier than expected, the study advanced to the second stage of Simon and non-futility was declared. Of the two patients that did not achieve a RECIST 1.1 response, 1 patient had progressive disease within 7 weeks of entering the study and the other patient had a decrease of -24.1% of their target lesions at 13 weeks (a RECIST 1.1 SD). This patient is currently ongoing with their study treatment . In stage 2, an additional 18 responders are required in a maximum of 32 patients but based on the current data the probability of success is expected to be ~90%. Cohort 2 is ongoing.

Table 1 demonstrates the profile of patients, and the key prognostic factors are shown. All patients had metastatic (stage IV) unresectable melanoma. The predominant site of metastases is the lung (n=6), but patients also entered the study with metastases in the liver, distant nodes or musculoskeletal. Two patients had metastases in both the liver and the lung.

Of the five patients that had reached the week 19 imaging timepoint, all five patients showed a sustained reduction in the overall tumour burden and this durability of response was also seen in four patients reaching week 25 and two reaching week 37 imaging timepoints. In the two patients that had reached week 37 the shrinkage was between -87 and -94%. The responders at week 13 are ongoing with their study treatment and will be observed for the total study period of 2 years.

Reassuringly, the addition of the SCIB1 to the standard of care ipilimumab with nivolumab did not enhance the toxicity of the checkpoint combination therapy in the patients evaluated to date. The safety evaluation is ongoing.

Conclusions

SCIB1 is well tolerated, and the ORR efficacy data of 82% in the first stage of cohort 1 is highly encouraging. This level of effectiveness in the combination setting has trailblazing potential for the ImmunoBody® platform in further improving the survival rates in patients with unresectable melanoma. This study is ongoing, and a phase 2/3 registration study is currently under planning.

Contact

Prof. Lindy Durrant
Scancell Ltd
robertmiller@scancell.co.uk
Website: https://www.scancell.co.uk
Phone:+44 (0)1865 582 066

References

Patel PM, Ottensmeier CH, Mulatero C, et al. Targeting gp100 and TRP-2 with a DNA vaccine: Incorporating T cell epitopes with a human IgG1 antibody induces potent T cell responses that are associated with favourable clinical outcome in a phase I/II trial. Oncoimmunology. 2018;7(6):e1433516.

Abstract Presentation Number: 1533